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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/077,392	02/15/2002	Kathryn F. Sykes	UTSD:557USD2	4223

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EXAMINER	
AKHAVAN, RAMIN	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/077,392	SYKES ET AL.	
	Examiner	Art Unit	
	Ray Akhavan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-62 and 97-109* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-62 and 97-109* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Information Disclosure Statement

Acknowledgment is made of the Information Disclosure Statement (IDS) filed 15 February 2002. A signed and initialed PTO 1449 form is mailed with this action. However, there are no translated documents corresponding to references B1, B3 and B4 in the file. These references are not considered.

Priority

Applicant's claim for priority is defective. This application is a division of Application No. 09/535,366, filed 03/24/2000, which claims benefit of a provisional Application No. 60/125,864 filed on 03/24/1999 and also claims benefit of a provisional Application No. 60/127,222 filed on 03/31/1999. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 120 as follows:

First, there is an error in referencing the provisional application filed on 3/31/1999: applicant's amendment to the specification indicates application no. "60/127,22" instead of 60/127,222, as is presumably intended. Furthermore, to perfect the claim for priority under

§120, applicant is required to point out the current status of all non-provisional applications in the first sentence of the specification.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

For the purpose of examination the priority date is **03/24/99** corresponding to provisional application no. 60/125,864.

Specification

The title of the invention is not descriptive. The title merely states LEEs and CEES, but the invention is directed to a method of assaying for biological function using linear or circular expression constructs. A new title is required that is clearly indicative of the invention to which the claims are directed.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. *See* Spec. at 30 ¶2 and 95 ¶2. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The disclosure is objected to because of the following informalities: the specification contains a typographical error on p. 5, line 4, where the word "may" is used in place of "many". Appropriate correction is required.

Claim Objections

Claims 60-62 are objected to because of the following informalities: Claims 60 and 61 are improperly dependent on a subsequent claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. **Claims 55, 57, 59-62, 100, 102, 104 and 108 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

Claims 55 and 57 contain the trademark/trade name PCR®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a process used in obtaining a DNA segment, accordingly, the identification/description is indefinite.

In addition claim 57 is vague and unclear because as written, it seems to be missing a modifier to clarify the relationship between deoxyuridines and uracil-DNA glycosylase (UDG). The claim is drawn to complementary stretches in the primer comprising deoxyuridines and UDG. The claim should be rewritten to indicate that UDG is acting on the deoxyuridines and is not itself contained in the primer. Furthermore claim 57 is vague in that there is no antecedent basis for the term "the non-covalent-linkage".

Claim 59 is vague because of the phrase, "more than one *type* of linear or circular expression element...". It is unclear what applicant means by "type". Are there different types of linear or circular expression elements, or does applicant mean that both linear and circular expression elements can simultaneously be introduced into the cell. It is unclear what other types of molecules are encompassed here.

Claims 60-62 are vague with regard to the phrase, "further defined as", because it is unclear what this phrase means in the context of a method of screening for a biological response.

Furthermore, it is unclear how further defining a screening method for a biological response as a method for producing antibodies or vaccinating an animal, further limits the claim. In addition the claims recite methods of producing antibodies or vaccinating animals but provide no method steps where this is accomplished.

Claim 102 is vague in the phrase "expression element comprises polymerase chain reaction...". It is unclear whether applicant means to say that PCR is a component of an expression element, which it clearly is not. It would be remedial to include "using" after the term "comprises".

Claims 100 and 104 are rejected as being vague and indefinite because they recite "eukaryotic terminator" and "eukaryotic promoter" respectively. However it is unclear from the specification or the claims whether applicant means promoter/terminators that are from a eukaryotic cell or those that function in eukaryotic cells. The specification indicates that the promoter and terminator may be from any source (Spec. at p. 5, lines 1-5). As written the metes and bounds of the claims are indefinite. For the purpose of examination viz., prior art, the claims will be interpreted as broadly as reasonable, which would mean any promoter/terminator capable of functioning in a eukaryotic cell.

Claim 108 uses a term "cell" to mean an animal, which is contrary to the accepted meaning of an animal – a multi-cellular organism. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d

1029, 1033 (Fed. Cir. 1999). The term "cell" in claim 108 is used by the claim to mean "an animal", while the accepted meaning is "a single cell." The term is indefinite because the specification does not clearly redefine the term. The specification does expand the definition of cell to mean "cell line" or "cell culture", but the disclosure does not define a cell to be an animal. (See Spec., at 28, ll. 15-24).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claim 54-57, 59, 97-104 and 106-109 are rejected under 35 U.S.C. 102(b) as being anticipated by Rashtchian (Curr. Opin. Biotech. 6:30-6 (1995))(see whole article).

Applicant's invention is directed to a method of screening for a biological response in a cell that is transformed/transfected with an expression construct (linear or circular), involving assaying for any open reading frame (ORF) encoded in the expression construct. In addition the claims are drawn to DNA segments being obtained through polymerase chain reaction (PCR) or chemical synthesis, followed *in vitro* linking or noncovalent linking of segments (e.g. ORF to promoter or terminator) to form expression constructs that are provided to cells, whereby a biological response is produced. More specifically the noncovalent linking involves obtaining a PCR product comprising stretches of deoxyuridines which are then acted upon by uracil-DNA glycosylase (UDG) to create overhangs to which promoter and terminator fragments with similar

overhangs can link to form expression constructs. Furthermore, the invention is directed to assaying for any biological response in any cell or organism.

Rashtchian teaches a expression constructs where the DNA segment or ORF is produced through PCR or chemical synthesis and noncovalently linked *in vitro*; the noncovalent process involves 5'tails containing deoxyuridine residues – every third base – which UDG subsequently acts upon to generate 3' cohesive termini that can be annealed (noncovalently) to complementary sequences in a suitable vector or another PCR-amplified DNA fragment (i.e. promoter or ORF containing terminator) (See p. 31-33 under section, Ligation-Independent Cloning and Fig. 1).

In addition Rashtchian teaches using T7 or SP6 promoters in constructing expression elements (e.g. Fig. 1). Both T7 and SP6 have been shown to be active either in eukaryotic cells or via eukaryotic polymerases. (See Kozak. Gene Expression. May 1991; 1(2):117-25, Abstract and p.119, col. 1, lines 6-12; Whetter et al. J. Virology. Aug. 1994; 68(8):5253-63, Abstract and p. 5255, col. 1, lines 7-12, 17-22) (note: these references are only provided to show the intrinsic characteristics of the T7 and SP6 promoter respectively, within the context of eukaryotic systems, thus they are not to be considered as an additional reference to be combined with Rashtchian).

Moreover, the expression constructs taught are made but for a single purpose – expression of a target product in a cell, where the target product has a biological activity or effect either directly or indirectly in the cell. In light of the foregoing teachings, Rashtchian anticipates the above noted claims.

3. Claims 54-55, 97-98, 100, 102-108 are rejected under 35 U.S.C. 102(b) as being anticipate by Ward et al. (Proc. Natl. Acad. Sci. July 1995; 92: 6772-77) (See whole document).

See supra under §102 rejections part two for a discussion of the subject matter to which the invention is drawn. Furthermore, the invention is drawn to a method of screening biological function by providing any cell an expression construct comprising an ORF that is expressible in said cell, such that a biological response is produced in the cell. In addition the invention is directed to producing an DNA segment or ORF through PCR or chemical synthesis as well as introduction of the expression elements to cells without intervening bacterial propogation.

Ward et al. teach expression constructs where DNA fragments are obtained either by restriction endonuclease digestion, chemical synthesis or PCR. (See e.g., p. 6773, col. 2, under Plasmid Constructions, p. 6776, Fig. 4). In addition Ward et al. teach an inducible promoter, i.e. vaccinia virus late promoter, linked to a T7 gene or HIV-1 envelope gene i.e. ORF. (e.g. p. 6774, Fig. 1 and p. 6776, ¶ 2 and Fig. 4) or linked to β-gal reporter gene (e.g. p. 6776, ¶ 2). Ward et al. teaches that vector backbones are ligated with DNA fragments (e.g. comprising target genes), with an intrinsic characteristic of ligation being linking in vitro as reflected in Figures 1 and 4. (See e.g., p. 6773, under Plasmid Construction, pp. 6774 and 6776).

Furthermore, Ward et al. teach terminators capable of function in mammalian cells (e.g. Abstract; p. 6773, col. 2, ¶ 2; p. 6774, col. 1, ¶ 2; p. 6776, ¶ 2). In addition Ward et al. teach providing expression elements to mammalian cells, i.e. BS-C-1 cells (e.g. p. 6773, col. 2, ¶ 2), under conditions where an ORF is expressed and a biological response is produced in the cell, i.e. β-gal assay. (e.g., p. 6776, under Discussion).

Moreover, Ward et al. teach using the vaccinia recombinant virus to express proteins in mammalian cells (e.g. p. 6773, ¶ 4 bridging to p. 6774), where BS-C-1 (mammalian) cells are infected with the recombinant virus (i.e. expression element) without any intervening bacterial propagation. (Id. and p.6774, col. 2, ¶1). In light of the teachings discussed above Ward et al. anticipate the above noted claims.

4. Claims 54-55, 58-62, 97-98, 100, 102-104 and 106-109 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnston et al. (U.S. Patent No. 5,703,057) (hereinafter '057 or '057 patent) (See whole document).

See foregoing discussion of the subject matter to which the invention is directed. In addition the invention is directed to injecting expression construct(s) into cells, more specifically, through microprojectile bombardment. Furthermore, claims are drawn to the method of screening for biological response, where the method is further defined as one that produces antibodies and that vaccinates an animal.

The '057 patent teaches a method of introduction of expression constructs into cells using microprojectile bombardment into mice (See e.g., col. 11, lines 25-52). The '057 patent further teaches that an expression library comprising various ORFs can be made using genomic DNA or using PCR to obtain cDNA from source RNA before linking to promoters and terminators to form expression constructs, all with the purpose of eliciting a biological (i.e. immunogenic) response in an animal. (See e.g., Abstract, col. 2, lines 61-67; col. 3, lines 13-16; col. 20, lines 49-62). In addition '057 teaches injecting multiple expression constructs into an animal (See e.g., Figs. 6 and -10, col. 10, lines 11-24), as well as using promoters and terminators capable of

function in eukaryotic systems (See e.g., promoters: col. 19, lines 36-56; terminators: Fig. 1A-D). Moreover, '057 teaches a method of screening for a biological response (i.e. immunogenic response) to a library of expression constructs where an open reading frame is linked to a promoter and terminator, where the protein is expressed with the ultimate goal of identifying and vaccinating an animal against a particular pathogen(s). (See e.g., Figs. 6 and 10, col. 2, ll. 50-60; col. 4, ll. 55-66). Suffice it to say that by definition, vaccines elicit an immune response involving antibody production in the animal being vaccinated. Pursuant to what '057 teaches, the claims above are anticipated.

Conclusion

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ramin (Ray) Akhavan whose telephone number is 703-305-4454. The examiner can normally be reached on 8:00-4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Remy Yucel, Ph.D., can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

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Ramin (Ray) Akhavan
Dec. 2, 2003

DAVID GUZO
PRIMARY EXAMINER